

THE MÜTTER LECTURES ON SELECTED TOPICS IN SURGICAL PATHOLOGY.

SERIES OF 1890-1.¹

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LECTURE III.

PYOGENIC ORGANISMS.

SYLLABUS. *Pyogenic Organisms*.—Obligate and facultative. Staphylococci; consideration of their varieties and common characteristics.

Streptococci.—Identity of those of pus with those of erysipelas. Comparison of the general characteristics of the two genera and of their peculiar activities. Distinction between erysipelas and allied, yet clinically different forms of cellulitis, etc.

Bacillus pyocyaneus.—*B. pyogenes foetidus*, etc.

Gonococci.—Included here, though not properly belonging here, since it is doubtful if they are truly pyogenic. Their relations to pus and to purulent mixed infection.

Pneumococci and Other Forms.—Bacilli tuberculosis, typhoid bacilli and other organisms rarely met with in pus. Table giving author's statistics of personal work.

A FEW years ago the known pyogenic organisms, or those which have the power of provoking the formation of pus by the destruction of exudate, could be counted on one's fingers. But the list now is greatly extended, and the organisms now known to be pyogenic belong to more than one genus,—belong not even in one kingdom, since they include both animal and vegetable forms. The former, however, pertain mainly to the lower animals, and man's worst enemies are principally bacteria.

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While then it would appear to be impossible to give in exact detail the name or biological position of every organism that has the power of producing pus, those subjoined below are by all means the more common forms met with in it. There is every reason to believe that there is not one of the pathogenic microbes which may not have the power, at particular times or under peculiar circumstances, of producing pus, yet there are a limited number of forms which are so invariably met with in it and which so uniformly have the power of producing it if they exert any action at all, that they are grouped in an arbitrary class under the name of pyogenic organisms. They are, of course, distinguished from each other, as are all other micro-organisms, by their microscopic appearance, peculiarities of growth, and their effects on animals. It has already been known for many years that organisms which, to the naked eye, in cultures, as well as when examined under the microscope, have every resemblance and appear to be identical, are yet capable of producing different effects in the living tissues. Possibly when our powers of observation shall be still further aided by some new device we may recognize some differences between them that at present we are unable to appreciate. For purposes of illustration, I have often put it in this way to students, that when we are at a distance from a crowd of human beings they all look alike to us, but that as we approach nearer we begin to notice differences of apparel and then of feature, so that we recognize friends or pick out strangers. So also one might tell the difference between two armies by the general color of their uniforms; and yet not be able to identify any particular organization. So it is in examining bacteria. Under the microscope alone all the pyogenic staphylococci appear alike. If we could get nearer to them, as it were, we might be able to distinguish between them. So, too, when we view an immense number of them on the surface of a nutrient jelly, we are able to distinguish one form from another by means of the particular color which they produce. The color of a culture by itself tells us no more about its distinctive organisms than does the color of an army seen at a distance, tell us what particular soldiers are engaged. We have certainly accomplished a great deal in the separation and

identification of individual organisms, the final and crucial experiments in most instances being upon animals.

The wholly arbitrary yet clinically justifiable classification of *pyogenic* organisms would be into the *obligate*, that is those which always produce pus if they are given time and have any effect at all, and the *facultative*, which apparently only at times cause suppuration.

THE OBLIGATE.

1. *Staphylococcus pyogenes aureus*.—The staphylococci are so called because they tend to arrange themselves in the form of clusters. They grow easily at ordinary summer heat, but most rapidly above 30° C. When grown in gelatine this variety causes liquefaction with the development of an orange-colored precipitate. Grown upon agar there appears within twenty hours a whitish or light yellow opaque tint which soon becomes more distinct, and of a bright orange. It presents the same appearance upon potatoes.

2. *Staphylococcus pyogenes albus*.—This organism is very similar to the previous one in the character of its growth, and in its effect on animals, but it produces no pigment. Observers differ in opinion as to whether it is more or less virulent than the aureus.

3. *Staphylococcus pyogenes citreus*.—This grows like the former, liquefies gelatine, and produces a growth at body temperature which presents a light yellow color, indistinguishable at first from cultivations of aureus, declaring itself some days later. In each case this pigment occurs only on exposure to air. Where it grows along the needle streak, in agar, there is no color reaction. The pathogenic properties of this variety are probably milder than those of the two before mentioned, though all three are pathogenic; by which term it is meant that the results of injections or experiments in animals is death. An organism which when injected into an animal makes it sick only and does not kill it, is not considered by bacteriologists as pathogenic. It behaves in most respects like the aureus and albus. When cultivations upon solid media are covered with a layer of oil, Passet found that their bright lemon yellow color was not produced.

An exact estimate of the relative powers of these three forms can hardly yet be made. It has also been claimed that the aureus after transmission through the bodies of several animals becomes changed into the albus, but I do not think that this claim has ever been substantiated, while the distinction between the aureus and the citreus seems sufficiently well established. There is every reason to think, from clinical experience, that the virulence of the same species differs within wide limits at different times, since results are gotten with them at one time by one observer which cannot be repeated by others. This seems to be especially true of acute infectious osteomyelitis. A special staphylococcus of osteomyelitis has been described by some writers, but the opinions of those best fitted to express them concur in the belief that it is really identical with the staphylococcus aureus, differing only in this unknown characteristic of virulence. This group has been studied chemically as well as biologically. Passet made some investigations into the chemical activities of these three pyogenic varieties. He found that the gelatine which they fluidify has a neutral, not an acid reaction. This is probably a transformation of gelatine into gelatine-peptone. According to Brieger these forms give off ammonia, while the streptococci produce trimethylamin. All of the cocci which Passet found in abscesses, as well as pure pneumococci and the cocci of erysipelas, cause a curdling of milk.

4 and 5. *Staphylococcus cereus albus* and *flavus* are the names of two varieties identified by Passet. Each grows with a wax-like layer on the surface of gelatine, and in patches on potatoes. In the one case this layer is white, in the other of citron-yellow color. These two forms are met with occasionally in pus from the human subject, although I believe never alone. They are not pathogenic in rabbits, and in many other animals, and are not supposed to be in man. The surface of their growths has a particularly waxy sheen, while along the needle track they both form a grayish white streak with fine beads.

6. Babes has described and named the *staphylococcus flavescens*, which probably occupies an intermediate position between the aureus and albus. It liquefies gelatine, and its

growth on agar becomes yellow after about eight days. It is pathogenic for mice.

7. *Staphylococcus pyosepticus*.—Richet has described a microbe which he found in a cancer in a dog, and which he named pyosepticus. It is distinguished from the albus by its effects on animals. It both produces pus and fatal general infection. It has a short life, and grows best at 38° C. Below 25° fluidification of gelatine does not occur until the seventh day; this is later than occurs with the albus. Also in beef-tea cultures there are recognized differences. In rabbits it produces great œdema within twenty four hours, while the albus produces only the slightest infiltration. Later fever, emaciation and death result. Inoculation in the anterior chamber causes rapid suppuration and destruction of the eye. Death seems to be produced by a ptomaine, and in most rapid cases within from ten to forty eight hours. In dogs injections are followed by phlegmon, and high fever. Evidently it is much less virulent in dogs than in rabbits. Guinea pigs and doves succumb quickly. By vaccination with reduced cultures, animals are given an immunity from the virulent material. In the blood it seems to perish quickly. In chronic cases it is found in colonies, especially in the liver. Experience with this organism in man has not been reported. (*Archiv. de Med. Exp.*, 1889, No. 5.)

Another peculiarity common at least to the pyogenic staphylococci is their wonderful vitality. They have the power of lying dormant in the tissues for months and years, and then of being aroused into activity by causes unknown, but such as accompany acute febrile or wasting diseases. Even in cultures they remain active for a long time. Old cultures emit a well-marked odor much like that of starch paste, and this odor can be frequently recognized in old dressings which have been saturated with pus. They more easily enter the blood current, and are by it more quickly disseminated. Phlegmons caused by staphylococci pursue a more rapid course both in time and in intensity of disturbance. There is no doubt at all in my mind but that collections of these organisms may hibernate, so to speak, in the bones, and possibly in other tissues, for twenty years, and then become again active, and exert sometimes a fatal degree of virulence.

According to all observers, the organisms which are most frequently met with in pus are the staphylococci, and of these most frequently the aureus, with the albus next. These are associated with acute abscesses, boils, acute osteomyelitis, etc., and their combination seems to be particularly unfavorable. Streptococci are also frequently present, but they are especially associated with erysipelas, or erysipelatoid processes, where suppuration occurs rather in the form of purulent infiltration, than from circumscribed abscess. They occur also, as was first pointed out by Ogston, in progressive gangrene, and are the chief or the most deadly organisms in pyæmia. Mastitis in women offers a good example of the different mode of action of these two species. Those mammary abscesses which are caused by staphylococci begin in the deeper part of the organ, and spread towards the surface, while suppurations which are caused by streptococci commence with an erysipelatoid affection of the skin, and extend from some crack or fissure of the nipple, the suppuration in the deeper part being secondary. The explanation is that the staphylococci act from the interior, spreading along the milk ducts, while the streptococci invade first the skin and spread along the lymphatic vessels. This statement is founded upon the demonstrations of Bumm, and is not theoretical.

Kitt has investigated similar disease in cows, and has cultivated a peculiar streptococcus from these cases, the injection of which sets up suppurative inflammation. In one case he injected pure cultivations into the milk ducts, with the result that in a few hours the corresponding portion of the udder became swollen, and by the next day it was acutely inflamed.

The clinical conclusions of Ogston, Rosenbach and Passet have been confirmed by Bumm and others, and may be stated about as follows: The staphylococci are the causative agents in primary and parenchymatous abscesses, while the streptococci are more disposed to excite peri-adenitis which shall terminate in abscesses. Bumm often found the former along with diverse non-pathogenic forms in fissures of the nipples, which do not accompany mastitis, and showed how they might thus penetrate even deeper and set up suppurative trouble. In at least one case he was able to demonstrate by sections, stained by Gram's method, that this had actually occurred.

Okintchitz thinks that the staphylococci have a tendency to sectional localization about the joints especially in pyæmic cases, and that the streptococci manifest a predilection for cellular tissue. In this respect he takes a diametrically opposite position to Krantzfeld and Pawlowski. The staphylococci are so frequently found along with other pyogenic forms, that it is hard to assign them their exact role.

In 1886 Bonome described three cases of pulmonary tuberculosis in which he recognized staphylococci as the active agent in producing secondary suppurat on, that is empyæma. In one case he recognized besides this form a diplococcus which he regarded as identical with Kleb's *micro sporon septicum*; so also in five cases of pulmonary gangrene he found them everywhere. On experimenting with pure cultures of the same germs made from these cases he succeeded in producing local gangrene at points of injection. He regards them as the active agents in causing the tissue necrosis, and holds the putrefactive features of these cases to be easily explained by the entrance of saprogenic organisms through the respiratory channels.

It has always been difficult, hitherto, to explain suppurative changes in the kidneys in scarlet and other eruptive fevers.

If we remember, however, that five years ago Fraenkel showed us how staphylococci were almost always to be found in the crypts of the tonsils, especially in cases of sore throat, it can readily be seen how they have ready access to the general circulation.

While, as we shall see shortly, there are differences of opinion as to the organisms most frequently concerned in producing pyæmia, and while the streptococci seem to be those especially to blame, we may as well mention here the results obtained by Pawlowski, who carefully examined five pyæmic cases. In one of these the metastatic manifestations were confined entirely to the joints. In this case he found streptococci alone. In the other cases he found staphylococcus aureus in the organs and soft tissues; results which tally well with those of Krantzfeld. One of his conclusions is worthy of repetition here: "These experiments lead me to the conviction that the staphylococcus pyogenes aureus is the active cause of pyæmia. For the development of the typical subacute form of pyæmia, there are required, indeed, beside the micro-organisms, decided disturbances of nutrition, such as fractures and general circulatory lesions."

Evidently a great variety of disturbance may be caused by the same organisms, this being due to causes some of which are still obscure. Thus, the staphylococcus aureus may cause a dermatitis, a boil, an abscess, acute ulcerative endocarditis, acute infectious osteomyelitis, or even pyæmia; while the streptococci cause sometimes erysipelas, and sometimes peritonitis, mastitis, puerperal fever, and even pyæmia also. Their varying action is not alone due to the numbers in which they are introduced, nor yet necessarily the locality where they are introduced. That they do not of themselves always set up abscess formation is evident from the fact that they are frequently present in the blood, while as yet no abscesses exist. They are even excreted in a living state by the kidneys without giving rise to secondary abscesses. In almost all cases of septic fever they may be found in the blood, and yet it is known that such cases frequently run their course without abscess formation. In acute osteomyelitis they are found in the blood, although there is no suppuration outside the bone.

Rosenbach has reported the case of a woman, æt. 30, married 10 years, with four children living, and healthy when born. Her fifth child, born at term, was, nevertheless, dead at time of birth, though apparently alive until shortly before that time. Attention was at once drawn to the right leg, which was swollen and showed fluctuation. The whole leg had an erysipelatous appearance, and much pus was evacuated. It was thought there had been necrosis of nearly all the soft parts of that leg, as well as of the bone. This is of interest as showing that the organisms which cause this acute gangrenous process must have been introduced through the blood of the mother.

A case occurring very recently under my own notice was that of a newly born child who rapidly developed an acute osteomyelitis of the right leg and thigh, as well as an extra capsular abscess about one shoulder, and who lived but a very short time after the disease declared itself. To be sure there was the possibility in this case that infection had proceeded from the umbilical cord, and yet there was absolutely nothing about the part to lead to the slightest suspicion.

Babes concludes that there is a difference between ordinary puerperal fever, which he considers a streptococcus invasion, and pyæmia following abortion, which he has found due to the staphylococcus pyogenes aureus. (*Prog. med. Roumain*, 1889, No. 24).

Escherich examined milk from nine healthy women without finding bacteria in it; also from five women suffering from non-puerperal fever, such as phthisis, syphilis, etc., and found no bacteria. In thirteen cases of puerperal fever once nothing was found in the milk, once bacilli were present, once other cocci were found only in the milk from one breast, while in ten the same organisms were present in the milk from both. In none of these was there any excoriation of the nipple, nor abscess in the glands. Staphylococci were the prevailing organisms. He believed that in these cases the organisms entered the blood from the uterus and were excreted with the milk. Numerous other facts show that organisms may circulate in the blood without necessarily giving rise to local disturbances.

Garré's experiment to prove the active agency of staphylococcus aureus in producing phlegmons is now a matter of history. He inoculated a little wound at the border of the nail and in two days noted suppuration there. Then he rubbed into his arm, as if it were an ointment, a quantity of pure culture of the third generation, and in four days suffered from a typical carbuncle, with consecutive swelling of the lymph glands. Recovery was a matter of several weeks and of numerous scars. (*Fortschritte d. Med.*, 1885, No. 6.)

One such experiment, by the way, on man, is of more value than many negative results on dogs, which only go to prove their immunity, or at all events, their high resistance.

Aside from Garré's personal case of abscess following inunction we have Bockhardt's experiment upon himself. He introduced a minute portion of cultures of aureus and albus into the skin of one of his fingers. In forty-eight hours a small abscess had formed, and was opened, and from its pus he recovered the aureus. On another occasion he inoculated by inunction a portion of the skin of his forearm, about the size of a silver dollar. After having cleaned and disinfected it, and slightly irritated it with his finger nail, he employed the same mixture as before. Six hours after rubbing it in, the skin was reddened and painful; eight hours later a number of pustules had formed; these pustules contained the cocci which he had employed, and within a week they had dried up and disappeared. Some days later he repeated the experiment by rubbing in a cultivation mixed with a sterilized salt solution. Twelve hours later thirty-five pustules had formed; within five hours more he saw twenty-five more form, most of them being perforated by hairs. After a week all had dried up except two, which developed into large and painful boils, and for two or three months after he was subject to a recurrence of pustules upon the skin of the same forearm. The fact that Bockhardt's results were milder than Garré's was due to the fact that the former employed a much more dilute culture.

These pustules were of an impetiginous character, not being preceded by nodules or vesicles. These are such as Wilson defined impetigo to consist of, and may occur anywhere except where there is much hair. In such situations Bockhardt thinks that if the same cause acts syccosis will result.

In Wilson's impetigo he has always found streptococci, and he holds that the impetigo pustule is often a forerunner of a boil, for it is often seated on and precedes it. His views are corroborated by Zuckermann's investigations.

Bumm injected pure cultures of staphylococcus aureus into the subcutaneous tissues of his own arm, and the arms of two other persons. The cultures were mixed

with a few drops of salt solution before injection. On each occasion a large abscess developed, whose pus contained large numbers of the same organism.

Schimmelbusch has demonstrated very beautifully how bacteria may work their way along the hairs into hair follicles and there cause furuncles. He rubbed into the unbroken skin (like Garré and Bockhardt) pure cultures of staphylococcus pyogenes aureus, by which pustules were produced. The skin was then excised, hardened in alcohol, its fat dissolved out with ether, then imbedded in celloidin, and sections made in series, which were stained by Gram's method and then with some contrast stain. A careful microscopical examination then showed that there was not the slightest injury to the tissues, but that the organisms had followed the hair shaft down into its follicle, and there proliferated, and that the infection of the tissues proceeded therefrom.

He found the same true of furuncles of spontaneous origin. The sweat glands do not have the same liability, since on the palm and the sole, where they most abound furuncles are most rare. On the contrary he finds them most common at spots where friction of dirty clothing or of ordinary soil is most marked; thus the back of the hands, the neck, the belly (from belts), etc. (*Archiv. f. Ohrenheilk.*, xxvii, 1889, 4, 252.)

8. *Streptococcus pyogenes—seu erysipelatis*.—By the term streptococci are meant those which arrange themselves in chains, sometimes of considerable length. They grow slowly on the ordinary culture media at a summer temperature, but at greater rapidity in beef tea and at body temperature.

On gelatine they form small, round, colorless colonies, which spread scarcely, if at all, on the surface. On agar they grow in small points but very slowly, and when sown on agar along a needle streak the growth is found, after weeks, to have extended but a very trifling distance. They do not liquefy gelatine, but in the absence of oxygen exert an energetic peptonizing action. When first described we heard considerable about two forms, namely: the streptococcus pyogenes, and the streptococcus erysipelatis. It is the latter which was so carefully and beautifully studied by Fehleisen, and demonstrated to be the active agent in the production of erysipelas. Observers are now pretty generally agreed that these two forms are identical. Individual cocci in any of these chains, of whatever species, are not necessarily of the same size. We have here another illustration of the fact already alluded to that the streptococci, which are so pathogenic in men, have very much less virulent properties in the lower animals. Fehleisen's coccus will not kill mice, rabbits nor guinea pigs. Moreover, it does not grow on the blood serum of calves,

hogs nor guinea pigs, but only on the serum of rabbits among these smaller animals. Nor does it grow in the bodies of these animals. It must be said, however, that the attempt from these facts to formulate a general rule that cocci grow only in the bodies of animals on whose serum they thrive, would not be justifiable.

In the present connection we are speaking of the one form to which the two different names have been given. Although from eight to ten different sub-species of streptococci have been carefully studied, all of which grow alike and look alike, yet they possess widely different pathogenic properties. Thus the streptococcus which by some is alleged as the cause of diphtheria looks and grows like all the rest which have no such power. Thus too, Behring has identified a sub-variety which he calls the streptococcus *murisepticus*, because it kills white mice in from forty-eight to sixty hours. This, too, was isolated from diphtheritic membrane, and, except by experiment on animals, can not be differentiated from other forms. In beef tea they all grow precisely alike.

The view that Fehleisen's erysipelas coccus is entitled to rank as a true pyogenic coccus is confirmed by Hoffa, who found it in the pus from a knee-joint whose overlying skin presented an erysipelatous inflammation. According to this view it is not necessarily nor invariably pyogenic, but may act in this way. De Simone also has reported the case of true pyæmia following an unmistakable erysipelas, in whose metastatic abscesses a small coccus was found, which tends to corroborate the same view. He also lays stress on the many remissions of temperature met with in cases of pyæmia, as well as erysipelas, in connection with the fact that the streptococcus erysipelatis grows to best advantage at temperatures below 37°C., and that at 41°C., after forty-eight hours, in cultures, it dies. According to this view the high temperatures noted at times in clinical cases may be a conservative or eliminative factor.

Hajek, differing from Baumgarten and others, considers the streptococcus of erysipelas and phlegmon not to be identical, although they cannot be distinguished by culture differences, since he says the principles of growth in the living body are not the same. He studied two cases of erysipelas, which were complicated with in-

tra-thoracic lesions. In one there was a sero-fibrinous pleuritic exudate in which he found a streptococcus having all the peculiarities of Fehleisen's. The other was a fatal case of so-called erysipelas-pneumonia, *i. e.*, pneumonia following erysipelas. In this case he found only Fraenkel's pneumonia-coccus. Fraenkel himself has quite recently made a careful study of the points of similarity between the streptococcus pyogenes or phlegmone, and that of erysipelas. He finds that neither morphologically nor in cultures, nor by color-reaction, can they be truly distinguished. He found the most beautiful growths in bouillon cultures. They behave alike in coagulating milk, and upon glycerine agar they grow alike. In experimenting upon animals no real distinction can be made, at one time phlegmon, at another lymphangitis, *i. e.*, erysipelas being called out. In thus recognizing their virtual identity, he simply fortifies the position already taken by Bionde, Eiselsberg, Kurth, Winkel and others above quoted, and especially that occupied by Baumgarten in his large work.

Passet's studies concerning the retention of life of all these pyogenic cocci so far mentioned, agree very well with Rosenbach's, and are in accord with general experience. In jelly staphylococci will live a year or so, while streptococci do not last more than three months. Drying either of them on glass for ten days does not destroy their vitality. Even a heat of 99° C. for fifteen minutes does not certainly kill them.

The experiments of Schuetz in connection with the disease in horses known as strangles are significant. The disease occurs under two forms; it begins as a nasal catarrh, and in the milder form is followed by suppuration of the cervical and sub-maxillary glands, and of those around the pharynx. In the severe form metastatic abscesses occur throughout the body, and the animal dies of a form of pyæmia. On examining the pus from these abscesses Schuetz found a peculiar streptococcus constantly present. These he cultivated on horse-blood serum, and was able to reproduce the disease by injecting a pure culture into the nasal cavity. These organisms are also pathogenic for mice.

Aside from the streptococci above mentioned, Hueppe separated and cultivated still another form, which he met with in a case of puerperal fever. This organism formed typical arthro-spores, similar to those of leuconostoc, and did not grow in nutrient jelly, but did grow well on blood serum. It will thus be seen to have been specifically different from the ordinary streptococci. It hardly seems necessary to rehearse at this point or in this place, all the varieties of pyogenic streptococci. Enough has been said to show that they at least have many common properties, and that as yet we have really no accurate way of distinguishing between them.

In general it may be said of them that they possess even more virulent properties than the staphylococci, and, indeed, their presence in large numbers is in some degree an index of the violence and acuteness of the case. If it were permissible to argue by analogy of biological form and properties, a marked illustration of the severity of disease, called out by

cocci which to a large extent resemble each other, might be found in such diseases of animals, as chicken-cholera, hog-cholera or swine-plague, rabbit septicæmia and, perhaps, some others. It is uncertain as yet whether these diseases can be inoculated at all upon man. They are at all events certainly acute and infectious enough in the animals mentioned.

GENERAL REMARKS UPON THE PYOGENIC COCCI.

Staphylococci and streptococci produce a peptonizing ferment by which albumen, even when coagulated, may be dissolved; and it is by virtue of this property that we have many of the phenomena attending suppuration. In milk they rapidly produce lactic acid, and this same lactic fermentation takes place sometimes in wounds, causing acidity of discharges, and in abscesses causes the well-known watery pus. (Cheyne). In our list of ptomaines produced solely in pure cultures of known species, we find none ascribed to pyogenic cocci; and they are not yet known to produce them; consequently fever attending suppuration can hardly be ascribed to this source. But, as Baumgarten suggests, it may be due to increased tissue change, due to their growth, the products thus formed being, perhaps, pyretic. Baumgarten supports this hypothesis by adducing the fever which occurs in trichinosis, where the question of ptomaines has not yet been raised.

Fehleisen is further of the opinion (*Arbeiten a. d. Chirurg. klin. Univ. Berlin*, III, 1887,) that the pyogenic cocci are not so much parasites in an actual sense, like anthrax bacilli, as agents for transportation of some injurious substances. He would explain the varying degrees of intensity of progressive suppuration and sepsis production rather by variation in strength or amount of the toxic material which they carry. In this matter he is decidedly opposed by those who believe these differences are to be explained rather by specific difference in activity which these organisms seem at different times to manifest. This latter view is borne out by analogy, since we see anthrax and tubercle bacilli evincing wide variations in specific energy under varying circumstances.

Okintchitz has carefully studied a number of cases of septic infection and pyæmia. (*St. Petersburg. Inaug. Dissert.*; Abstract in *Manchester Med. Chron.*) In his cases of so-called septicæmia he has failed to make the distinction between sapræmia and septicæmia which I shall endeavor to show is a legitimate and an important one, though he admits they deserve different names. In his cases of septic poisoning (*i. e.*, sapræmia) the patients' blood did not contain any pus microbes, though they were easily detected about the primary foci. But he did find in the

blood of one of his septicæmic cases a peculiar microbe, which he considers identical with Bardoni-Uffreduzzi's *proteus hominis capsulatus*; in another he found Fraenkel's diplococcus and the staphylococcus pyogenes albus. In a number of cases of phlegmon he found one or other staphylococcus form (in a few of them in the blood), though only by culture experiments and not with the microscope. He shows, however, that their appearance in the blood seemingly has little connection with the intensity of fever or oscillations of temperature, and that the most pronounced clinical difference between the mycotic and the non-mycotic changes consists apparently in gastric disturbances, which are present in the former (mycotic) variety.

His pyæmic cases showed invariably either staphylococci or streptococci in the blood, which could ordinarily be recognized even with the microscope. Organisms thus found in the blood showed fission or reproduction very rarely as compared with those found in the pus of the primary foci, hence the supposition is justifiable that their reproductive activity is mainly confined to pus and not blood: hence also the great practical importance of thorough disinfection and destruction of primary and other foci. He considers that great numerical strength of hæmic microbes has a very unfavorable prognostic significance (*vid.* Eiselsberg's studies, Lecture, II), even in the absence of metastases about internal organs, the converse of this being also true. He thinks too that the bacillus pyocyaneus is rather a constant follower of the streptococcus, belonging more to the saprophytes, and invading it if prepared for it by other bacteria.

Manfredi and Traversa would seem to have discovered the explanation of certain peculiar symptoms, coma, cramps, etc., noted occasionally in severe cases of erysipelas. They experimented on numerous animals with bouillon cultures of the streptococcus erysipelatis which had been sterilized by filtration. They found that there were remaining in the solutions apparently two ptomaines, one having the property of producing paralytic pneumonia, the other of causing cramps and epileptiform convulsive movements. These ptomaines seemed best formed when oxygen was excluded, oxygen seemed to reduce them.

I have, for years, endeavored to find a pathological basis for the clinical distinction which an accurate diagnostician should make between genuine erysipelas, whose biological cause is well known, thanks to Fehleisen, and cases of what may be and often is called *cellulitis*, or perhaps the *erythema exsudativum multiforme* of Hebra.

I have made cultures and examinations from a number of these latter, and while I have never found such uniformity of results as would permit me to draw any permissible conclusions, so far as specificity is concerned, I can at least say that

such cases as run a different clinical course are in all probability pathologically different. That is to say that I have never found erysipelas cocci when this disease failed to declare itself clinically. On the other hand I have found in these other cases sometimes nothing, and once or twice either staphylococcus forms or some organism whose identity I failed to make out.

This is quite in accordance with Cordua's studies. (*Zur Ätiologie des erythema multiforme, Deutsche med. Woch.*, 1885, No. 33, p. 576.) He investigated fifteen out of one hundred and twenty-seven cases of skin affection of the hand and fingers resembling erysipelas. Its resemblance as well as the fact that it was met with in patients peculiarly exposed, *e. g.*, cooks, butchers, cyster-openers, etc., led him to undertake the examination. From these fifteen patients he excised small bits of skin and placed them upon agar in the oven. From these he obtained a coccus resembling staphylococcus pyogenes albus save that it was three or four times larger. Upon animals it was inactive. He twice inoculated himself, with the result that at each point he produced a dark red swelling of the skin resembling the original disease. He likens it to Rosenbach's "*Finger-erysipeloid*" without establishing its identity therewith; and is rather of the opinion that different organisms may produce the same cutaneous disturbance.

Two years later in *Langenbeck's Archives*, 1887, Rosenbach more fully described the cutaneous disease which he termed *erysipeloid*, which appears much like Cordua's *erythema multiforme*. The microbe of this disease Rosenbach first supposed to be a coccus, but after studying it further determined that it belonged to the chladothrix group. It grows best on gelatine at 20° C., but very slowly, and in this medium it most resembles in growth the bacillus of septicæmia of mice. In form it is like the cladothrix dichotoma, but smaller. By inoculation of a pure culture Rosenbach produced an attack of erysipeloid upon his own arm.

Repeated endeavors to implant it upon lupous skin, in order to eradicate the specific ulceration, were fruitless.

9. *Bacillus pyocyaneus*.—This is the organism which occasionally gives to pus its greenish or bluish tint. It is one of the most active of the pyogenic germs, and up to the present has only been found in connection with man. That the organism is of some importance and interest to pathologists, is evidenced by the recent work of Charrin, "*La Maladie Pyocyane*," which appeared in 1889. Ledderhose was among the first, perhaps the first, to establish that the bacillus pyocyaneus, which had hitherto been supposed to be simply a saprophyte, was in effect a pyogenic organism.

About the same time Pawlowski showed the same fact, and it was found that Koch had learned that it was fatal when in-

jected into the peritoneum of the guinea-pig. While the statement above made, as to its never being met with except in man, is true, it nevertheless has powerful pathogenic properties when inoculated upon the lower animals.

Ernst has distinguished two varieties of this bacillus, which he denominates alpha and beta. They agree in morphology, but he has described a peculiar "chameleon phenomenon," which only the beta form presents in potato cultures. When such a growth upon a potato is disturbed with a needle, in from two to five minutes a change of tint is discovered, the reddish brown tone merging into a leaf-green. This seems to be so constant as to constitute a genuine point of distinction and to furnish a possible argument in favor of Naegeli's views concerning the mutability of species.

This organism, as it grows, generates a coloring matter which gives as characteristic a tint to cultures as to the pus, and which has been isolated by Fordos and been called *pyocyanin* (vide Lecture I.). This is a crystallizable substance; beside it another substance called *pyoxanthin* has been isolated by the same observer. Pyocyanin in alkaline solutions gives a blue, or in acids a red tint. A third coloring matter has been described by Babes, which gives by transmitted light a reddish brown, by reflected light an emerald green tint. It is soluble in water, and insoluble in chloroform. In acid solutions it gives a steel gray color. When these are made alkaline, the dichroism returns. It appears to be composed of two separate ingredients, one of which is soluble in alcohol, the other not. He also separated an aromatic substance whose odor reminds one of linden blossoms. These studies he made upon the beta form of Ernst. Pyocyanin is the most easily studied of these various substances, and is only mildly, if at all toxic. Minute crystals of it can be sometimes seen upon the surface of cultures. Its formation is not a regular nor a necessary accompaniment of the growth of the bacillus; it grows only under peculiar conditions, and the secretions of the skin appear to favor its formation.

10. *Bacillus pyogenes fætidus*.—Passet found this organism in an abscess in the neighborhood of the rectum. It is by no means peculiar to peri-intestinal abscesses, however, since I have myself once found it in an abscess of the brain, and have met with it in abscesses from other localities. It is a short,

plump bacillus, which forms a white surface growth, and gives off a disgusting odor. On potatoes it forms a brownish mass. It does not liquefy gelatine. It grows in milk, but does not generate an odor. It is pathogenic in mice and guinea-pigs, but not in rabbits. The injection of a few drops of culture in the former animals causes septicæmia.

FACULTATIVE PYOGENIC ORGANISMS.

The gonococcus.—This organism figures, of course, most prominently as the sole cause of true or specific gonorrhœa. Discovered first by Neisser, it has since been the subject of a vast amount of study, of which the most fruitful part has perhaps been done by Bumm. He, more than any other, has demonstrated its specificity, and has stamped gonorrhœa as ranking among our best known parasitic diseases.

The gonococcus is a coccus, commonly met with in pairs, otherwise a diplococcus, presenting a double-biscuit shape or arrangement which of itself is quite distinctive. It is never found in chains, but frequently in tetrads, though it is not regularly thus grouped like the micrococcus tetragenus.

Nuclear stains, like the basic aniline dyes, do not make a deep impression on these cocci. Such stains as vesuvium or Bismarck-brown may answer well enough for cover glass preparations but do not suffice for sections. It is noteworthy, and in certain respects a valuable diagnostic point, that they lose their aniline stain when prepared according to Gram's method. While they share this peculiarity with certain other forms they may be differentiated from the pyogenic cocci by this sign, which consequently is of value.

Their most marked peculiarity is their power of penetrating living protoplasm and propagating there. Scarcely any, perhaps none, of the other pathogenic cocci have this property. In examining gonorrhœal pus the pus-cells will be seen to contain numerous groups of diplococci, which may have proliferated so rapidly as to completely fill the cell.

The gonococcus is well nigh the most difficult of all the common bacteria to cultivate. At first it was believed that the gonorrhœa-germ would grow upon the ordinary nutritive gelatine; then it was found that this was an error, and that they would grow only upon coagulated blood serum, or gelatine-

serum, and furthermore that they thrive to best advantage only upon human-blood-serum.

It has been claimed that upon agar to which has been added 2 to 5% of Kemmerick's peptone they could be cultivated, but it has been found that this statement is not in accordance with fact. Also upon potato it can be scarcely grown. Even upon a suitable medium it is most difficult to cultivate.

It must be deposited in relatively large quantity and in pretty pure form. That is, if planted along with common pyogenic cocci they appear to prevent its growth. The temperature must be maintained at 33°-37° C. and new cultures must be made from day to day. The cocci die out in two or three days in cultures. Nevertheless Sinnety and Herneguy (*Progres Medical*, 1885, No. 33.) have shown that they may live inside the living body after the active disease has been apparently subdued by antiseptics; since in some of their patients they found the cocci a year after the apparent subsidence of the disease. The well known statements of Noeggerath are in perfect accord with these.

The investigations of Neisser, Bockhardt and Bumm make it indisputable that gonococci call forth an active purulent discharge from the mucosa of the genito-urinary tracts. They penetrate between the epithelial elements to the papillary layer. By the second day a lively emigration of the white corpuscles begins. The epithelial layer is thereby elevated from its base, and between them is formed a fibrinous exudate, exceedingly rich in cells, which later are loaded with cocci. Epithelial regeneration, in the average case, begins in four days and should be fairly complete in twenty. It appears that mucous membrane which is covered with cylindrical epithelium is most likely to suffer from this parasitic attack (urethra, uterus, glands of Bartholini, conjunctiva), while that provided with flat epithelial cells (mouth, nose) for the most part escapes.

According to Bockhart the acutest period of an attack of gonorrhœal catarrh is that during which there is the liveliest contest between the gonococci which have penetrated the mucosa and submucosa and the numerous leucocytes that are a part of the copious exudate which infiltrates the connective tissue.

The whole history of a gonorrhœal attack exhibits that we have to do with an irritative cause affecting a surface, as in the case of erysipelas, which in both cases commonly disappears without leaving permanent injury to the tissues; and that it is only exceptionally that the deeper tissues suffer, or those of internal organs by secondary localization. Such complications as epididymitis, endometritis or salpingitis are caused by spreading along continuous surfaces.

Bumm has done more than any one to study the nature of gonorrhœal mixed infection. The most common contaminating agents are the pyogenic cocci. Such mixed infections can take place in the female:

1. In Bartholini's glands. Here not only pyogenic but saprogenic cocci as well as the gonococcus can easily penetrate. Abscesses as well as retention cysts may occur here.

2. In the urethra. Urethral abscesses of either anterior or posterior wall occur by means of infection of the glands.

3. In the bladder. A true primary gonorrhœal infection of bladder epithelium is not known. The cystitis is of pyogenic origin and usually an extension from the urethra.

4. In the cervix. Suppurative parametritis is the analogue of acute gonorrhœal bubo in the male, which is always due to pyogenic action. Whether it is truly an infectious or an irritative process is yet an open question.

5. In the so-called gonorrhœal rheumatism (arthritis), which, as manifested especially in the knee, yields a fluid which shows a mixed infection.

6. Tubal-tuberculosis is probably often to be regarded as really a gonorrhœal mixed infection.

Indeed it is scarcely even doubtful whether such destructive lesions as those which lead to formation of stricture or suppurating bubo can be caused by gonococci alone; on the contrary it is extremely probable that these never occur without the participation of the common pyogenic cocci. The experiences of numerous observers, the writer included, show that the staphylococci are often to be found in the urethra, and such rare cases as one which I have elsewhere reported (*Jour. Cut. and Venereal Disease*, December, 1888, p. 441) show that pyæmia following gonorrhœa is not unknown, while the true

pyæmia itself is not to be explained except by the action of the common pyogenic organisms. In fact one may accept the general statement that gonococci exert a true pyogenic action only upon certain mucous surfaces; and that beneath such surfaces they do not find the conditions necessary to their growth. They are ærobie in high degree, and it would appear that only epithelium and not connective tissue cells possess the required chemical character. Bumm found that injections of pure gonorrhœal pus into the tissues were harmless, as were also pure cultures. Indeed if 24 hours after injections of such material we cut into the part and remove some of this same pus we shall find that while pus cells still remain the gonococci have disappeared. This is a matter of great interest, showing that pus cells—apart from the bacteria which they contain, do not exert a pyogenic action. (Vid. Lect. II.)

Kitt has determined an analogous fact in connection with the mastitis of cows. The peculiar organisms only exert their pathogenic action when they are present in the ducts or acini of the gland, *i. e.*, upon its epithelial covering; if injected directly into its tissue they cause no suppuration.

Bockhart, in 1886, described a “pseudo-gonorrhœal urethritis” of moderate severity only, caused by a diplococcus that was met with also in vaginal secretion when it was *not* of acid but of alkaline or neutral reaction. It has nearly the same biscuit form as Neisser’s coccus, is very small, is met with sometimes alone, sometimes in groups of two to six, usually in the fluid and not in the cells. It does not collect in such clusters as does Neisser’s coccus. It grows on agar at 30°-32° C., but better on serum. Inoculation on the healthy urethra in two instances evoked a mild urethritis. In connection with this form of urethritis he describes also a “pseudo-gonorrhœal epididymitis.”

Schwarz does not hesitate to express himself very positively that gonorrhœa is the only infectious catarrh of the female genitals; the bearer of the contagion, or rather the contagious element itself, is Neisser’s gonococcus. Any secretion in which it is not found is not so. Without gonococci there is no gonorrhœa; all manifestations of gonorrhœa are connected with its activity; they are pathognomic evidences of the disease. (*Die gon. Infection beim Weiber, Volkmann’s Saml. kl. Vort.*, No. 279.)

But this view of Schwarz fails to account for numerous cases of “bastard-urethritis” where inflammation runs high, where bubo is common, but where Neisser’s coccus is not found in the

pus. That these cases present sufficiently acute features will be attested by numerous patients. Whether these are provoked by Bockhart's diplococcus, or whether an acute urethritis can be engendered by staphylococci is not yet determined.

In the *Centblt. f. allgemeine Pathologie*, Vol. i, No. 18, Pellizzari has made a contribution toward corroborating the view that there is no real abscess produced by the gonococcus, but that all the suppurating buboes, and other abscesses appearing to be provoked through the influence of the organism are in reality mixed infections. He reports three cases of peri-urethral abscesses which appear to have been caused, as usual, by extension of the inflammation from the urethra into one or more of the urethral follicles, in all of which the pus proved to be a mixture. His paper constitutes interesting reading, and serves as a further corroboration of views already expressed.

The most significant other feature of true gonorrhœal disease is its occasional sequelæ in the shape of post-gonorrhœal arthritis, whose most conspicuous sign is an effusion into the joint cavity. This sometimes is a thin serum, and sometimes it is quite fibrinous or flocculent.

In 1885 I read that Petrone had recognized gonococci in this fluid. Soon after this I demonstrated this discovery by preparations from a patient of my own. Kemmerer, Affanasiev, Bergmann and Smirnoff, as well as others, have done the same thing. In view of such discoveries it would appear impracticable to explain these arthritides—or at least all of them—upon the ground of reflex irritation from the urethra, although there is no denying that we do meet with joint effusions after mere catheterization. Of course true suppurative arthritis is only to be explained by the theory of mixed infection already alluded to.

The pneumonococcus.—Two or three different organisms have been described under this name. That, for instance, of Friedlaender, which has a capsule, and that of Fraenkel which grows like Sternberg's coccus from saliva, and perhaps one other form. This organism certainly is not commonly pyogenic, but that it may prove itself so occasionally is placed beyond doubt by the investigations of several observers. For instance, Fraenkel, like Talamon and Salvioli, has found his pneumonococcus in cases of empyæma following pneumonia, and has come to the conclusion that this sputum-septicæmia coccus is a common and frequent cause alike of pneumonia and

of these subsequent diseased conditions. It concerns us most in this relation to know that under certain circumstances it may show a true pyogenic activity. It has also been found in pus from cases of combined pneumonia and meningitis, the intracranial pus being found to be a pure culture of the microbe. These statements are corroborated by Foa and Bordoni-Uffreduzzi.

Gabbi and Puritz have identified the diplococcus of Fraenkel in the pus from a peri-articular abscess occurring in a case of acute pneumonia. Pus from this abscess injected under the skin of a rabbit produced acute septic symptoms, of which the animal died. In its blood the same coccus was also found. This appears to be the first case of peri-articular inflammation recognized as being caused by Fraenkel's pneumonia coccus. Hitherto only cases of arthritis have been described by Weichselbaum, Belfanti, Monti and Santer, all of whom have found it in pus from the interior of joints in complicated croupous pneumonia. (*Centblt. f. Bakt.*, viii, No. 5.)

Injections of it into the knees of animals have almost invariably produced purulent arthritis. After injecting cultures into neighboring tissues, and then injuring the joint surfaces with sterilized needles, thus making a point of least resistance, the results were less certain though frequently successful. Gabbi compares the inconsistency of these results with the great infrequency of joint complications in pneumonia. Weichselbaum found this same coccus in three cases of peritonitis. In one of them it followed a pneumonia; in the second a double pleurisy; in the third it was idiopathic. It will be remembered that Fraenkel's coccus is the same as the *micrococcus Pasteuri* of Sternberg.

In the early part of this century it had been noted by Dr. B. W. Dudley, of Kentucky, that during an epidemic of typhoid pneumonia which devastated the central portion of his native state many cases were followed by a "bilious fever characterized, like the plague, by a tendency to local affections. Abscesses formed among the muscles of the body, legs and arms, and were so intractable that limbs were sometimes amputated to get rid of the trouble."

The pseudo-pneumococcus of Passet.—He found an organism in the pus of acute abscesses, which closely resembles Friedlaender's pneumococcus. He met with it once in a small acute abscess of the back, and once in pus from the knee joint of a patient who sickened and died of croupous pneumonia. In the former instance he found it alone, in the latter in connection with other organisms.

It forms grayish-white, semi-circular elevations on the surface of gelatine, and in the earlier stages of growth is indistinguishable from Friedländer's coccus, but at a later period recognizable differences appear both as regards growth and effect upon animals. In pure cultures it does not grow along the needle streak, hence it is ærobic. On potatoes it gives off no gas, and mice inhale it without disturbance. Injected into the pleural cavity of mice and rabbits, it causes pleuritis. When injected subcutaneously it often produces abscesses in mice and rabbits, while Friedländer's coccus is not pathogenic for rabbits.

Micrococcus pyogenes tenuis.—This was first described by Rosenbach, who found it in three cases of deep suppuration. Since he described it not a single observer has met with it till Dr. Maria Raskina, of St. Petersburg, succeeded in isolating it from the pus and organs of an infant dying of severe scarlatina, complicated with pyæmia, on the 18th day.

The pus from the metastatic abscesses was found to be almost a pure culture of this coccus, while the parenchymatous juice of the various organs contained beside it a large diplococcus of unknown biological position. Inoculations of pure cultures of the pyogenic coccus under the skin of rabbits gave negative results, though the blood of the animals showed the presence of the coccus for at least twenty hours after injection. Hence the true pyogenic power of the organism is somewhat problematical, Rosenbach's researches failing to demonstrate it. Dr. Raskina considers that it may belong to the group of so-called *metabiotic* microbes of Garré; that is that it occurs only secondarily after suppuration has been caused by some other coccus. Nevertheless she states, as above, that the pus from her case seemed almost a pure culture of this same organism. (*Trans. of the Third Gen. Meeting of Russian Physicians*, 1889; Abst. in *Manchester Med. Chronicle*.) On agar it forms an extremely delicate, well nigh invisible layer. The individual organisms are somewhat irregular in shape, and average larger than the streptococcus pyogenes.

Rosenbach's oval coccus.—This observer found in one case of acute suppuration an oval coccus, which rapidly liquifies gelatine, and produces pus when injected into the eyes of rabbits. It has not been further studied, nor even given a name.

The glanders bacillus (Bacillus mallei).—Rudenko after carefully studying the lymph glands in cases of lymph-glanders produced abscesses by injection of pure cultures of glanders. The pus from these abscesses he also found to be a pure culture of the injected microbes. Consequently we must include this organism among our pyogenic forms. He always found the neighboring lymph glands to be infected with them.

Bacillus of malignant œdema (Vibrio septique).—Whether the bacillus of malignant œdema really deserves to be grouped with pyogenic organisms, is not yet known. It has been found in pus, however, as, e.g., a very interesting report by Braatz shows.

In a case of progressive gangrenous emphysema of the cervical region he evacuated a quantity of very offensive, gaseous, sero-purulent fluid. In this fluid the bacillus was found along with staphylococci and streptococci. The most interesting feature of this case is that the patient, an ignorant peasant, had a swelling under the jaw first, and then, by advice of his wife, drank a glass of chamomile tea in which he had put a table-spoonful of rat fæces. When we remember the liability of the rat to this disease we seem to see an explanation for the development of the same in man.

The bacillus tuberculosis.—This organism is not commonly enumerated as among the pyogenic, yet it is indisputable that it can produce abscesses whose contents are pure cultures. Thus, for instance, Fraenkel has carefully reported a case of brain abscess in whose contents the tubercle bacillus was the only organism found. That such collections of pus were not originally mixed infections is apparently proven by the fact that they become infected with pyogenic organisms so soon as they became exposed, as by incision.

It is hardly credible if one group of staphylococci, for example, had exhausted the fluid contents of such a cavity and then died out in it, that another group could later live and thrive in the same fluid. Fraenkel's deduction was warmly contested by Baumgarten, who claimed that he did not prove his case, that he no doubt had a tubercular focus in the brain, but that its detritus was not true pus, but pseudo-pus, consequently that the tuberculous bacilli were not entitled to be considered as truly pyogenic. However Baumgarten's objection must fall in the light of the reasoning above given. Whether such organisms as the tuberculosis bacillus shall produce abscesses or not is largely a question of time. In virulent *milzbrand* the poisoning of the system is too rapid, and the animal dies before the anthrax bacilli have time to act, but when a Guinea-pig is inoculated with attenuated virus, and then dies six, eight or ten weeks later, one finds not only infarcts and metastatic processes, but multiple abscesses whose contents are pure cultures of anthrax bacilli. The same is known also of the typhoid bacillus, of the pneumonococcus, of the bacillus of tetanus, and this general statement also holds good for

tubercle and for septicæmia. We have *foudroyante* forms where the specific element kills before abscesses have time to form, and we have other slow forms with the well known abscesses. In all these cases it is not so much a question of the pyogenic powers of certain bacteria, as of the time during which they are permitted to act. The bacillus of tetanus, for instance, is never found without the presence of pus, so far as I know, at least in the human organism, yet its main influence lies not so much in its pyogenic as in its tetanizing powers. The bacilli get into the divided cord of the new-born from the midwife's rusty shears, or dirty hands, or from the dirty rags bound around it, and the tetanus of the new-born in no sense differs from the traumatic forms.

Tetanus bacillus.—Inasmuch as it is proposed to devote a good portion of Lecture V. (q.v.) to this organism, it will be unnecessary to do more than to simply mention it here as among the facultative pyogenic species.

Typhoid bacilli.—When, later in this course, I shall, as I hope, take up the topic of *Mixed Infection*, I shall have more to say upon these bacilli as pyogenic organisms. Golzi had opportunity to observe a case of acute osteomyelitis during the course of a relapse of typhoid fever, and in the pus found typhoid bacilli and no other organisms. He then experimented with pure cultures of bacilli, and found that if he first broke the femur and then injected them he determined an abscess at the seat of fracture nearly every time. He concludes that these organisms are much more disposed to produce suppuration in rabbits than in man. (*Lo Sperimentale*, June, 1890).

Orloff has devoted no little time to a careful study of the suppurations which complicate typhoid. (*Centrblt. f. Bakteriologie*, 1890, viii, No. 12, p. 366, from *Wratsch*.) They occur most frequently in the skin-boils, in the subcutaneous areolar tissue-abscesses, particularly when there are pressure-sores; also as abscesses of the larynx in the connective tissue around the trachea and in the mediastinum; less often in the muscles (rectus abdominalis and glutæi), the more external lymphatic glands, the thyroid and salivary glands and the bones and joints. The latter terminate sometimes in diastasis, and sometimes in exostosis or suppuration. Sometimes one

bone or joint suffers, sometimes several; more commonly in younger patients. The exudate is sometimes serous, at others sero-purulent or absolutely purulent. Of internal suppurations perhaps the more common is empyæma, though abscesses occur in liver and spleen; these suppurations are not grouped with disintegrations of mesenteric glands, nor with rupture of splenic or ovarian infarcts.

Investigators generally incline to the view that most of these suppurations are really mixed infections, though undoubtedly typhoid bacilli alone may provoke formation of pus.

But Orloff decided to settle this matter by a series of experiments which could not be mistaken. He undertook (1) to determine by injections of pure cultures whether typhoid bacilli could call forth pus; (2) whether, if so, it was by virtue of their own presence or by their products, and whether, if not, the injection of mixed cultures produced any modification by action one upon the other. These experiments appear to have been conducted with most scrupulous attention to details, which, however, it is hardly necessary to describe just here. His conclusions were carefully deduced from amply sufficient data and bear the stamp of reliability. They are:

1. Injections of typhoid bacilli (pure cultures) into various tissues (joints, muscles, etc.) produce active round-cell infiltration and violent suppuration.
2. The same results, though much less acute, follow injections of sterilized cultures; whence follows that:
3. The chemical products of these organisms are, at least in no inconsiderable degree, the causes of these manifestations.
4. Suppurations occurring during typhoid or during convalescence, whose pus contains only typhoid bacilli, depend entirely upon them for their provocation, and are not to be regarded as mixed infections.

Further confirmation of this view comes occasionally also from yet other sources. Thus, Achalme (*La Semaine médicale*, 1890, No. 27) reports a case of periostitis of the tibia as a sequel of typhoid. Typhoid bacilli were found in the pus and no other organism.

Micrococcus tetragenus.—This is an organism from the mouth, known to be present in pulmonary abscesses in consumptives, as

a contamination So far as I know the first recognition as a form which *per se* could produce pus was a case which I reported in *The Medical News* in 1888. It occurred in a young woman with a peculiar form of submaxillary and cervical phlegmon of exasperatingly slow course, in the pus from which I found this coccus and this alone, and in which the path of infection from a badly diseased tooth could be traced.

It is known to possess pyogenic properties in certain small animals.

Zuckermann, writing in 1887, condensed the results obtained from a study of 495 acute abscesses. According to these staphylococci were found in 71 %, and streptococci in 16 %. In 5 1/2 % both were found together. In the balance of cases other forms were found. These results vary but little from the more recent studies of Steinhaus.

Some two or three years ago I presented to the American Surgical Association a table showing my findings in about 50 purulent cases. I have since more than trebled the number, but present herewith a table of only 100 cases, in which, among other things, will be found, *e. g.*, my justification for some of the statements made in the previous lecture. (Absence of organisms in the archepon of cold abscesses, etc.) These 100 cases are selected only in this respect, that I am prepared to vouch for the accuracy of the results; which we cannot always do. (See Table).

Anthrax bacilli.—These, as a rule, especially in man, do not alone provoke suppuration, but abscesses which contain them appear to be the result rather of mixed infection.

But there is some reason to think that even in man, and much reason to believe that in animals they may, exceptionally, act in a purely pyogenic capacity.

Actinomycosis.—Pathologists were for some time in doubt as to whether actinomycotic abscesses were not all truly mixed or secondary infections. This matter I believe is now set at rest, and it is definitely settled that rarely these fungi provoke suppuration without aid from other organisms.

Szénásy, in the first case of actinomycosis recognized in Hungary, met with a painful fluctuating swelling of the right mamma. By aspiration he withdrew tenacious pus in which were found typical actinomycotic forms; which were also found in the sputum. (*Centbl. f. Chir.*, 1886, No. 4.)

TABLE.

Disease.	No growth.	<i>Bacillus pseudo-pneumonicus</i>	<i>Bacillus coli communis</i>	<i>Bacillus of Erem pus</i>	<i>Bacillus ure liquefaciens</i>	<i>Bacillus fluorescens putridus</i>	<i>Bacillus anthracis</i>	<i>Bacillus fluorescens liquefaciens</i> ..	<i>Streptococcus erysipellatis</i>	<i>Micrococcus tetragmus</i>	<i>Bacillus pyogenes faecidis</i>	<i>Streptococcus pyogenes</i>	<i>Staphylococcus cereus flavus</i>	<i>Staphylococcus cereus albus</i>	<i>Staphylococcus pyogenes citreus</i>	<i>Staphylococcus pyogenes aureus</i> ..	<i>Staphylococcus pyogenes albus</i>	Number of cases.
Abscesses.....	32	15	21	2	5	2	1	1	1	1	1	1	1	1	1	1	1	32
Caries.....	3	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Necrosis.....	7	3	4	1	2	1	1	1	1	1	1	1	1	1	1	1	1	7
Ulcers.....	4	2	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	4
Ulcer, sy hilitic.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chancroidal pus.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Pus from bubo.....	4	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	4
Discharge from chronic gonorrhœa.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Pustules.....	5	2	4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5
Carbuncle.....	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Phlegmon.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cellulitis.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Erysipelas.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Felon.....	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Empyema.....	6	1	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	6
Gangrenous phlegmon.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Tetanus.....	3	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Pyæmia.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Hypopyon.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Gall-bladder abscess.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Abscesses, cold.....	9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	9
Hæmatoma, material from.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Tubercular testicle.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Tubercular lymphnode.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Enlarged thyroid.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Central osteo-myelitis.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Tuberculosis of bone.....	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Post-operative sarcoma.....	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total.....	100	41	38	6	12	7	11	2	1	2	1	2	1	1	1	1	1	118

The writer must here express his indebtedness to his previous assistant, Dr. Matzinger, and his present assistant, Dr. Bergtold, for most of this work.

Aspergilli.—The same is true of two varieties, at least, of *aspergillus*; and it is claimed that *spirochæte* may provoke suppurative otitis media.

In 1877 Grawitz described a purulent inflammation in rabbits' eyes which he had experimentally created with this fungus. In 1881 he injected it into rabbits' blood and subsequently recovered it by culture methods from the liver, kidneys, etc., and demonstrated for the first time that it might act as a pure pyogenic organism.

And were we considering suppuration in animals rather than in man we should have to include such microbes as those which cause contagious acne in horses, the various septicæmiæ in different animals, etc.

Following I purpose to mention, without attempt to classify them specially, several forms of organisms which have been met with in pus from various human sources. In 1885 Tilanus reported two cases of compound fractures of the leg, which ended in gangrene. From the gangrenous tissue of one he separated a new bacterium which he termed *bacillus gangrenæ*; from the second another, to which he gave the name *micrococcus fætidus*. After experiments therewith and failure to get any inoculation results, he regarded them as saprophytes, rather than pathogenic microbes, which, nevertheless, generated the ptomaines by which the patients were fatally poisoned.

Kartulis has found in fresh pus from abscess of the liver consequent upon dysentery, the dysenteric amœba which he had previously described as having been found in cases of acute and chronic enteritis among the Egyptians, but along with it were found the common pyogenic cocci, and he makes no claim that the amœba had anything like a pyogenic action. This naturally calls to mind the recent discovery of Prof. Osler, who has, within a year, reported a number of observations on pus from hepatic abscesses in which could be still seen active and moving amœboid organisms. Enough study has not been given to these, so far as I know, to permit a statement as to whether they are or are not in effect pyogenic organisms, though I presume that they are.

A few years ago Netter determined that after ligature of the ductus choledochus, the previously sterile contents of the gall-bladder contained bacteria, and by ordinary methods he made out two species of organism, one the well known staphylococ-

cus pyogenes aureus, the other a short bacillus, which he, for the first time, described, and which he identified as the same which he and Martha found in an hepatic abscess consequent upon gall-stone (*Archives de Physiol. norm. et pathol.* 1886, No. 5, p. 7). This case was complicated with ulcerative endocarditis, and the same bacillus was found in the cardiac valves. They regarded it as an inhabitant of the intestine which wandered into the gall duct, favored by the obstruction above, then into the liver tissue, and thence into the blood, causing both the abscess and the valvular lesion. They found, furthermore, in literature five other cases of combined biliary obstruction and verrucous or ulcerative endocarditis, and they consider that this bacillus possesses possible pyogenic properties.

Netter, in this latter communication, claims that hepatic abscesses, caused by staphylococcus alone, are accompanied by others in other organs, while those caused by his peculiar bacillus are marked by a lowering of temperature, even to 34° C., and cellular changes in the liver. In mixed infection we have a combination of symptoms. Injections of staphylococcus cultures produce the now well known pyogenic effects; injections of cultures of his bacillus caused disseminated, hyaline degeneration of liver cells. He has also met with this bacillus in the biliary passages of another patient after biliary obstruction, without abscess, beside the case reported by himself and Martha. (*Progrés Médical*, 1886, Nov. 13. p. 992.)

It occurred to me last winter to meet with a case of abscess of the gall-bladder from which I removed 104 gall-stones, in the pus from which I found a bacillus which tallies in every respect, so far as I can learn, with that described above by Netter; having only Netter's somewhat vague description to go by, I am unable, positively, to identify it as the same, though I have no doubt of it.

Hauser (*Ueber Faulnisbakterien und deren Beziehung zur Septicæmie*, Leipzig, 1885) describes three forms of saprophytic bacilli, which he terms *Proteus vulgaris*, *Proteus mirabilis* and *Proteus Zenkeri*. They are characterized in part by a certain pleomorphism, which he, perhaps, unduly exaggerates, and by a peculiar "schwarmstadium," by which is meant that in 5% gelatine they make sudden and extensive changes of locality,

that they *swarm*, as it were. That they are certainly saprophytic in action, he placed beyond a question. He further showed that they produce a very active ptomaine, which, in small quantities, exerts a marked toxic effect, causing in living animals all the phenomena of putrid intoxication, increased pulse and temperature, emesis, cramps, cyanosis, collapse and death. That they possess pyogenic properties is not demonstrated. It, moreover, appears that they are not harbored nor nurtured in the living tissues and fluids of healthy animals.

Chantemesse examined carefully a few cases of Delhi boil ("*bouton du Nil*"), and isolated a coccus which, in many respects, resembled the staphylococcus pyogenes aureus, but which was slower in liquefying gelatine and more quick to assume a yellow tint, and which grew a little differently on potato.

Inoculated upon two human arms, in pure culture, it produced each time a furuncle, which changed to an ulcerating nodule, the ulcer being crateriform, and rapidly healing under sublimate dressings. The pus from this furuncle was a pure culture of this "microbe du clou du Nil." Upon rabbits it was sometimes rapidly fatal, sometimes produced chronic lesions, resembling those upon men. (*Annales de l'Institute Pasteur*, 1887, No. 11). This must be consequently reckoned as one of the pyogenic forms.

Netter investigated twenty five cases of suppurative meningitis. Four times he could trace it to aural disease, once each to the sphenoidal and ethmoidal cells. In eleven cases it was metastatic, the primary focus being twice in the placenta, once in the pleura, and eight times in the lungs. He found the following bacteria which he considered as the active agents in producing the suppuration:

Diplococcus pneumoniae in sixteen cases.

Streptococcus pyogenes in four cases.

Diplococcus intracellularis in two cases.

Bacillus pneumoniae (Friedlaender?) in one case.

A short mobile bacillus, identical with that found by Newman and Schaffer in meningitis, in one case.

A small curved bacillus that could not be cultivated, in one case.

He consequently maintains that suppurative meningitis can be caused by *various* bacteria, whereof the diplococcus pneu-

monia is most common. He, further, thinks it possible to distinguish the bacterial factor by the clinical course of the disease, and the character of the exudate. When the diplococcus pneumoniae was found the exudate was green and viscous; when the streptococcus was found it was less adherent and more sero-purulent.

Other investigators have found the diplococcus pneumoniae in twenty-seven cases of forty-five examined, the streptococcus six times, the diplococcus intracellularis ten times, and the bacillus of Newman and Schaffer once.

This latter form much resembles the typhoid bacillus, morphologically, yet is distinct. Its discoverers claim that sterilized cultures of it cause not the slightest local disturbance; consequently the idea advanced by Grawitz and DeBary that ptomaines are unnecessary for the production of pus seems to be scarcely borne out in this instance, since this is a pyogenic agent.

While throughout these lectures and without evasion, we have taken the position that *there is, clinically, no suppuration without the action of microorganisms*, we must also insist that this expression is not intended to imply *bacteria* alone, since such other living organisms as that of actinomycosis, several of the molds, and the amœboid organism recently described by Osler, can produce it. And in the lower animals it is probable that numerous of the protozoa, as well, can provoke it. It has been stated that the injection of metallic mercury under the skin, especially of syphilitics, will produce the same result, though when the evidence to this effect is sifted, it is not found to be above criticism.

But in an inquiry of this kind it is not so important—though still most interesting—to study the rarely or unusually and uncommonly pyogenic organisms as to determine, if possible, under what circumstances the well-known pyogenic forms produce pus.

In 1861 Verneuil expressed the idea that liquids contained in the hernial sac contained toxic or irritating matters. In 1867 Nepveu found cocci in such fluid. At the *Congres de Chirurgie*, in 1889, Clado, of Paris, took up the question. In the contents of a sac which had contained a strangulated her-

nia (fatal one hour after operation), he found numerous mobile bacteria. The next day, at the section, these were found in the blood, lungs and spleen. In the strangulated knuckle there were the same microbes as in the blood, lymphatics and glands. The cultures furnished one special bacterium which, cultivated at 28° C., proved inoffensive, but cultivated between 37° and 40° became mortal within a few hours. Inoculation into the blood caused death in series. It was particularly pathogenic for guinea pigs and rabbits. In the dog it caused vomiting and loss of appetite followed by recovery. It multiplied in bodies of animals with astonishing rapidity. Clado accounts for the rapid death of some hernial cases by its penetration into the economy, taking its starting point from the surface of the intestine. Visceral congestions, so frequently observed, are the result of its localization, particularly in the lungs. Post-hernial peritonitis is held to be due to its migration through the intestinal parietes, the distention of the knuckle by gas being supposed to favor mechanically their penetration into the mucous membrane.

Bönnecken has carefully examined the fluid contained in the sac in eight cases of strangulated hernia in men, as well as in several dogs in whom it was artificially produced. In every one there were found numerous micro-organisms which proved to be identical with those ordinarily found in the intestine. A venous stasis appeared to be the pre-requisite for first the escape of fluid and then its infection. Beside the ordinary bacterium, he met with Miller's *micrococcus aerogenes*, and Escherich's *streptococcus coli brevis* and *gracilis* and *bacterium lactis aerogenes*. These bacteria were also found in the tissues and on the serous surface.

The circumstance that these same forms were found in the peritoneal cavity and in the heart's blood, means that death was caused by peritoneal sepsis and absorption of poison before pus had time to form. The author consequently holds a careful disinfection of the sac and the included loop or loops of intestine, before relieving strangulation, to be urgently indicated. (*Virchow's Archiv.*, cxx.)

Abundant corroboration of the practical value of this deduction comes from many sources. Velpeau showed that the fluid contained in the sac of an incarcerated or strangulated hernia produced an irritating effect upon the hands of the operator, and many observers since him have noticed that the escape of this fluid into the peritoneum gives rise to peritonitis without there having been any injury to it sufficient by itself to produce it. The investigations of Clado confirm those of Bonnecken; when he inoculated dogs with this fluid or its con-

tained bacteria he produced rapid death, with symptoms of violent intoxication.

Verneuil has given to this condition the excellent name of stercoral intoxication.

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